

MAY 21 1999

Receipt
Attorney Docket No.:MSA-004.01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Duff et al.)	
)	
Appl. No.:	09/247,874)	Art Unit: 1643
)	
Filed:	February 10, 1999)	Examiner: Not Yet Assigned
)	
For:	Therapeutics and Diagnostics Based on a)	
	Novel IL-1B Mutation)	

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Carmen Parra
Carmen Parra

**Application Processing Division's
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Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

REQUEST FOR CORRECTION OF FILING RECEIPT
AND
REQUEST FOR CORRECTION OF CERTIFIED COPY

Enclosed is a copy of the Filing Receipt received from the United States Patent and Trademark Office for the above-referenced application. There is an error on the Filing Receipt. The title of the application should read **Therapeutics and Diagnostics Based on a Novel IL-1B Mutation**, as indicated on the first page of the application as filed (copy enclosed).

The correct information, adding **IL**, is shown in red ink on the filing receipt.

Applicants respectfully request issuance of a corrected filing receipt for this application. Applicants further request that the correct title be corrected on the certified copy of this application.

If there are any questions concerning this request, the Examiner is invited to contact the

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undersigned at (617) 832-1272.

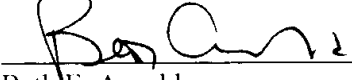
If there are any fees due in connection with the filing of this request, please charge the fees to our **Deposit Account No. 06-1448**.

5/21/99

May 21, 1999

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ATTY. DOCKET MSA-004.01

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THERAPEUTICS AND DIAGNOSTICS BASED ON A NOVEL IL-1B MUTATION

10 1. BACKGROUND OF THE INVENTION

Genetic testing (also referred to as "genetic screening" or "genotyping") involves the analysis of an individual's genomic DNA (or a nucleic acid corresponding thereto) to identify a particular disease causing or contributing mutation or polymorphism, directly or based on detection of a mutation or polymorphism (a marker) that is in linkage disequilibrium with the disease causing or contributing gene.

Early indication of a genetic predisposition to a particular disease provides an opportunity for medical intervention before the development of clinically characteristic symptoms. In addition, sophisticated genetic testing can in many instances differentiate individual patients with subtle or clinically indistinguishable differences, facilitating a more customized therapy. In addition, identification of a mutation can provide a target for identifying drug candidates.

Diseases and conditions, both monogenic and polygenic, for which diagnostic or prognostic genetic tests exist include: Cystic Fibrosis, Gaucher's Disease, Huntington's Disease, Duchenne Muscular Dystrophy, hemophilias, thalassemias, Alzheimer's Disease, breast, ovarian and prostatic cancers and periodontal disease. This list continues to grow.

The IL-1 gene cluster is located on the long arm of chromosome 2 (2q13) and contains at least the genes for IL-1 α (IL-1A), IL-1 β (IL-1B), and the IL-1 receptor antagonist (IL-1RN) within a region of 430 Kb (Nicklin, *et al.*, *Genomics* 19: 382-4 (1994)). The agonist molecules, IL-1 α and IL-1 β , have potent pro-inflammatory activity and are involved with the initiation of many inflammatory cascades. Their actions, often via the induction of other cytokines such as IL-6 and IL-8, lead to activation and recruitment of leukocytes into damaged tissue, local production of vasoactive agents, fever response in the brain and the hepatic acute phase response. The IL-1 receptor antagonist binds to the IL-1 receptor, but does not activate a signal. IL-1 α and IL-1 β proteins bind to type I and type II IL-1 receptors, but only the type I receptor transduces a signal to the interior of the cell. In contrast, the type II receptor may be surface bound or may be shed to become a soluble receptor. The bound type I receptor binds the agonist molecule but does not transduce a signal to activate the cell. The soluble receptors bind agonists and act as a decoy receptor. The receptor antagonist and the type II receptor, therefore, are both anti-inflammatory in their actions.

DATA ENTRY ST: 00000,

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